Respiratory Application Review

How the Lungs Work

- The air that you breathe in through your nose or mouth travels down through your trachea (windpipe) into two tubes in your lungs called bronchial tubes or airways.
- The airways are shaped like an upside-down tree with many branches. The windpipe is the trunk. It splits into two bronchial tubes, or bronchi. Thinner tubes called bronchioles branch out from the bronchi.
- The bronchioles end in tiny air sacs called alveoli. These air sacs have very thin walls, and small blood vessels called capillaries run through them.
  - ~300 million alveoli in a normal lung.
- When the air that you've just breathed in reaches these air sacs, the oxygen in the air passes through the air sac walls into the blood in the capillaries. At the same time, carbon dioxide (a waste gas) moves from the capillaries into the air sacs. This process is called gas exchange.
- The oxygen-rich blood in the capillaries then flows into larger veins, which carry it to the heart. Your heart pumps the oxygen-rich blood to all your body's organs. These organs can't function without an ongoing supply of oxygen.

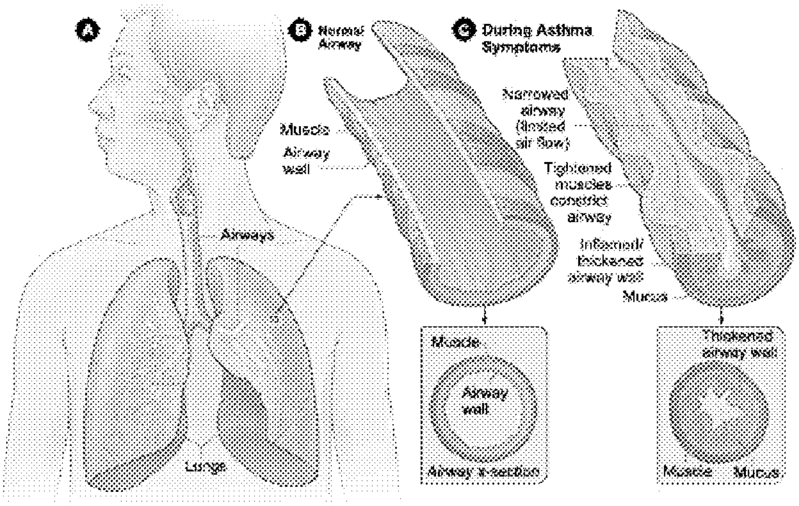
Disease Models: Asthma

- What is it?
  - Disorder that causes the airways of the lungs to swell and narrow, leading to wheezing, shortness of breath, chest tightness, and coughing
  - No cure
- What does it affect?
  - Affects airway resistance
- What is the primary cause?
  - Genetic and environmental factors
- How do we study it?
  - RC, NAM, WBP, PFT

Disease Models: Asthma

- Endpoints?
  - Primarily frequency (BPM), resistance/penH, flows
- Approach?
  - Aerosol exposure to a compound that elicits a response
- Typical species used?
  - Rodents

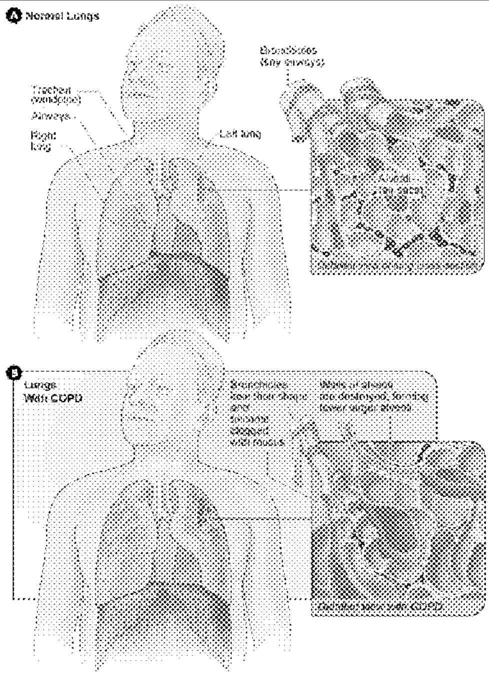
Disease Models: Asthma



Disease Models: COPD

- What is it?
  - COPD (chronic obstructive pulmonary disease) is a progressive disease that makes it hard to breathe.
  - Two primary conditions:
    1. Emphysema: Destruction of the lungs over time.
       - Walls between air sacs become damaged
         - Air sacs lose their shape and become floppy
       - Walls between air sacs become destroyed
         - Fewer and larger air sacs result in reduced gas exchange
         - Air gets trapped in damaged air sacs
    2. Chronic Bronchitis: Long term cough with mucus
       - Lining of airways is constantly irritated and inflamed
       - Causes lining to thicken and develop mucus
  - There is no cure for COPD

Disease Models: COPD



- What does it affect?
  - Affects lung compliance (elastance)
- What is the primary cause?
  - Cigarette smoke
- How do we study it?
  - RC, PFT, Smoke/Inhalation

Disease Models: COPD

- Endpoints?
  - Primarily frequency (BPM), compliance, volumes
- Approach?
  - Animal is diseased prior to any tests performed
- Typical species used?
  - Rodents

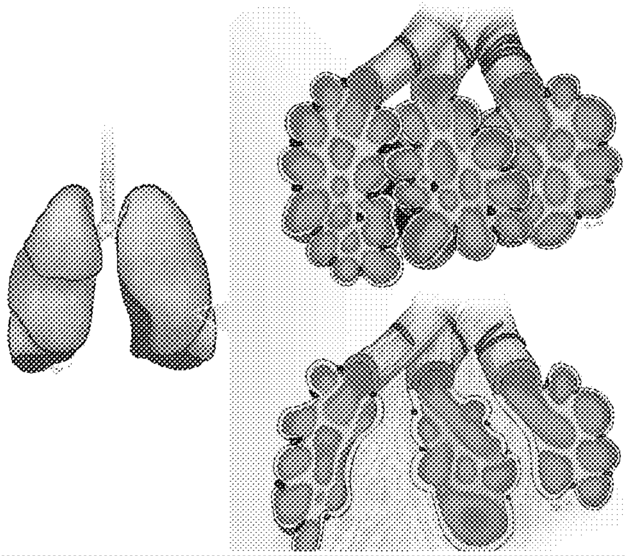
Disease Models: Pulmonary Fibrosis

- What is it?
  - Disease in which tissue deep in the lungs become thick, stiff, and scarred over time
  - No cure for pulmonary fibrosis
- What does it affect?
  - Lung compliance (decrease compliance – increased stiffness)
- What is the primary cause?
  - Over 140 known causes. Some are idiopathic (unknown). However, exposure to environmental pollutants and certain medications can cause the disease.
- How do we study it?
  - PFT

Disease Models: Pulmonary Fibrosis

- Endpoints?
  - Primarily frequency (BPM), compliance, volumes
- Approach?
  - Animal is diseased prior to any tests performed
- Typical species used?
  - Rodents

Disease Models: Pulmonary Fibrosis



Disease Models: Sleep Apnea

- What is it?
  - Common disorder in which you have one or more pauses in breathing or shallow breaths while sleeping
  - Two primary types:
    1. OSA: Obstructive sleep apnea (most common)
       - Airway collapses or becomes blocked during sleep; causing shallow breathing or breathing pauses
    2. CSA: Central sleep apnea (neural control of breathing)
       - Portion of brain that controls breathing does not send the correct signals to breathing muscles; resulting in no effort to breathe for brief periods

Disease Models: Sleep Apnea

- **What does it affect?**
  - Changes in sympathetic nerve activity
  - ↓ O2, ↑ BP, ↑ ST elevation, ↑ Ventricular asystole, enlarged atrium (↓ esophageal pressure, ↓ atrial pressure)
- **What is the primary cause?**
  - Over-relaxed muscles in throat and mouth
  - Tongue and tonsils obstruct windpipe
  - Overweight – fat tissue can thicken the wall of the windpipe
- **How do we study it?**
  - WBP performing chronic intermittent hypoxia tests (CIH)
  - CIH (in as little as 10 days) induces many cardio-respiratory behaviors as seen in OSA populations

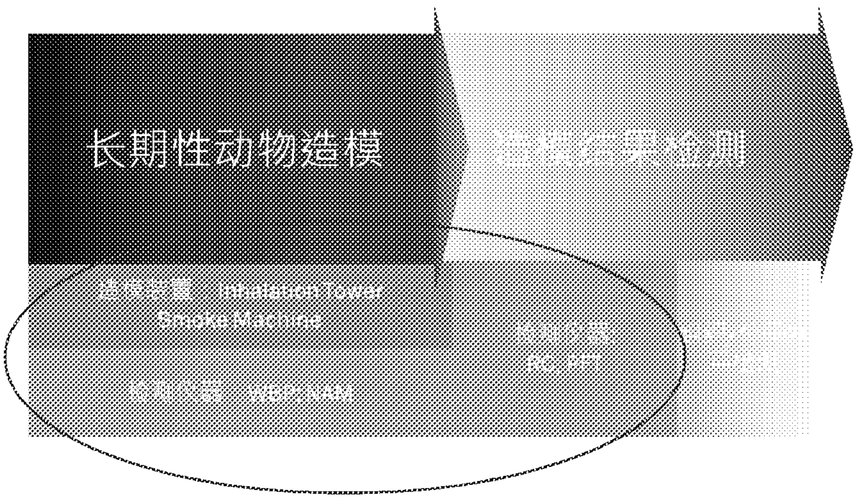
Disease Models: Sleep Apnea

- Endpoints?
  - Primarily frequency (BPM), volumes, and timing
    - Others:
      - Fractional Concentrations (of O2 and CO2)
      - Rate of O2 consumption (VO_2)
      - Rate of CO_2 production (VCO_2)
      - Respiratory Exchange Ratio (RER)
- Approach?
  - Intermittent exposure to hypoxia and normoxia conditions
- Typical species used?
  - Rodents

Pulmonary disease model summary

Goal	Effect
Asthma, allergy	Increase FRC Increase Airway Hyperresponsiveness (AHR)
COPD, emphysema	Increase Resistance Decrease conductance Reduce compliance Increase FRC
Cystic Fibrosis	Reduce FRC Reduce compliance
Sleep Apnea	Interrupted breath Respiratory rate
Inhalation	Monitor minute volume, respiratory rate Aerosol concentration Accumulated dose

一般动物呼吸研究



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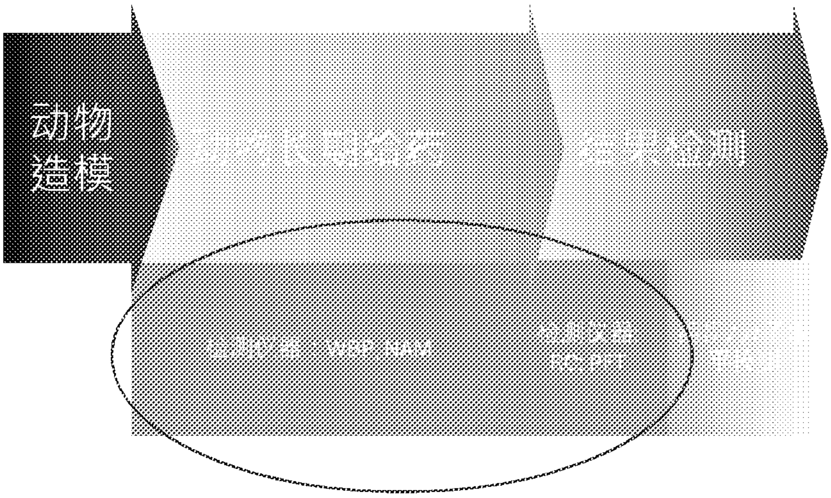


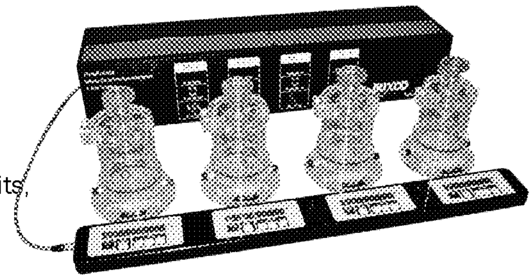
Respiratory Solutions

Parameters				
Volume	**Obstruction**	**Compliance**	**Conductance**	**Ventilation**
Tidal Volume (TV)	Lung Resistance (Rl)	Chord Compliance (Cchord)	FEV	Respiratory Rate (f)
Functional Residual Capacity (FRC)	Specific Airway Resistance (sRaw)	Dynamic Compliance (Cdyn)	FEV100,200,300,400,1000	Minute Volume (MV)
Vital Capacity (VC)	Enhanced Pause (PenH)	Static Compliance (Cstatic)	PEF	Accumulated Volume (AV)
Total Lung Capacity (TLC)	EF 50			Accumulated Dose (AD)

- Resistance and Compliance (RC)
- Non-invasive Airway Mechanics (NAM)
- Whole Body Plethysmography (WBP)
- Pulmonary Function Testing (PFT) – Forced Maneuvers
- Inhalation Tower – Exposure

Whole Body Plethysmography (WBP)

- Advantages
  - Subjects are conscious and unrestrained
  - Use for cough analysis
- Mice, Rats, Guinea Pigs, Rabbits, Ferrets, Dogs, Cats, Monkeys, Birds, Swine



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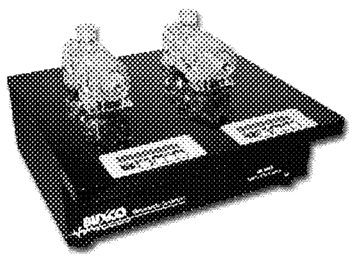
Non-invasive Airway Mechanics(NAM)

- Advantages
  - Continuously measures Specific Airway Resistance in conscious animals (sRaw)
  - No anesthesia
  - Built-in aerosol delivery and control



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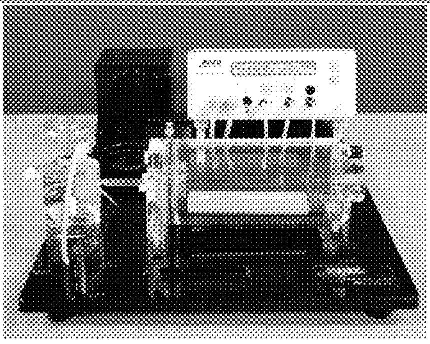
Resistance and Compliance (RC)

- Advantages
  - Continuously measures lung resistance and dynamic compliance in anesthetized animals
  - Heated bed
  - Optional heart rate or blood pressure monitoring
  - In-line aerosol delivery and control



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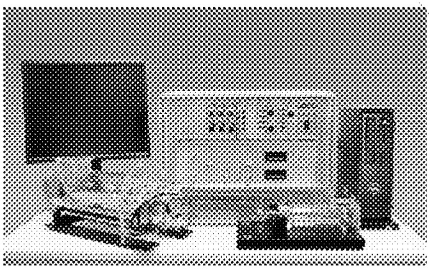
Pulmonary Function Testing (PFT)

- Advantages
  - The most comprehensive assessment of the lung
  - Determine FRC and other lung capacities
  - Complete a series of tests in just minutes
  - Ideal for COPD studies



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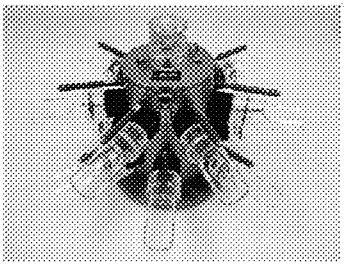
Inhalation (Exposure)

- Advantages
  - "Flow past" concentric design, so each animal receives the same exposure
  - Top and bottom ports, for delivering aerosols, gases and dusts.
  - Low dead-space nose adapters
  - Computer regulated core pressure



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Thank you!